REMARKS

Objections

The Examiner objected to claim 4 because of the grammatically incorrect phrase, "under the specified in claim 1." Claim 4 has been amended to state "under the conditions specified in claim 1." Claim 31 has been amended to incorporate the text of withdrawn claim 19, from which it formerly depended.

Rejection of claims under 35 U.S.C. § 112

Claim 3 is rejected under 35 U.S.C. § 112 as being indefinite due to the lack of limiting definitions of "conventional amination method" or "simple shoulder". The applicants submit those phrases would be readily understood by those skilled in the art in view of the specification. Nevertheless, Claim 3 has been amended to remove these phrases as unnecessary; part (ii) of claim 2 encompasses compositions yielding only a simple shoulder on the pneumosamine peak.

Rejection of claims under 35 U.S.C. § 102

Claims 1, 2, 5-7, 9, 10, 30, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Moreau. It is alleged that the process of reductive amination without prior borohydride reduction taught in Moreau yields a product inherently having the properties of the presently claimed pneumococcus polysaccharide. The applicants respectfully traverse.

As described more fully below,

(1) The methods of the present application produce aminated pneumococcus polysaccharides having no detectable compound X;

(2) Moreau does not teach the methods of the present application; and

(3) There are no teachings in Moreau or any other art even suggesting let alone definitively demonstrating that there *necessarily* is no detectable compound X in the conjugates produced by the method of Moreau.

To anticipate by inherency, the prior art must *necessarily* teach all limitations of the claims. The Office has provided no evidence even suggesting that the conjugates of Moreau *may* lack compound X let alone *necessarily* lack compound X. For this reason, Moreau cannot anticipate the present claims.

When a conventional reductive amination method is performed on pneumococcus type 5 capsular polysaccharide, the Sug residue of the base unit of the pneumococcus type 5 polysaccharide is converted into three compounds: N-acetylated β-D-quinovosamine, N-acetylated β-D-fucosamine, and a compound termed "compound X." Compound X is undesirable because it decreases the immunogenicity of the pneumococcus type 5 capsular polysaccharide (p. 7, lines 10-17). Pneumococcus type 5 capsular polysaccharide subject to conventional reductive animation manifests a ^{13}C NMR signal between 13 and 14 ppm, inclusive (p. 5, l. 37 – p. 6, l. 20) and/or a peak between fucosamine and pneumosamine in an HPAEC-PAD chromatogram.

An aspect of the present invention is methods that avoid formation of compound X. One method comprises reductive amination in the presence of a reducing agent selective for a Schiff base for a period between 30 min. and 4 hours in a specific range of pH that is between 4 and 6.5, longer periods of time resulting in the formation of the undesirable compound X. P. 8, ll. 19-25 and p. 17, ll. 14-34. A second method involves three successive steps: 1) reduction of the ketone function of the Sug moiety, 2) fragmentation of the reduced polysaccharide, and 3) reductive amination. P. 8, ll. 27-35 and p. 19, l. 16 *et seq.* Accordingly, a ^{13}C NMR signal between 13 and 14 ppm (p. 5, l. 37 – p. 6, l. 20) and/or a peak between fucosamine and pneumosamine in an HPAEC-PAD chromatogram are not observed.

Moreau does not disclose such methods. Rather, Moreau combines microwaving with methods of amination that, but for the duration of the amination, are otherwise conventional. These methods differ from the methods of the present application, and there is nothing in Moreau itself or any other art that suggests that Moreau's method would or could produce the presently claimed conjugates, which have no detectable compound X.

Moreover, while Moreau includes pneumococcus type 5 polysaccharides among those polysaccharides that can be aminated according to its method, Moreau never actually conducts its method on a pneumococcus type 5 polysaccharide and, therefore, does not teach an aminated pneumococcus type 5 capsular polysaccharide of any type. Consequently, for this reason as well, Moreau cannot anticipate the present claims.

In view of the foregoing, the applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of claims under 35 U.S.C. § 103

It is alleged that the presently claimed conjugates are *prima facie* obvious because Moreau teaches a method for the reductive amination and Jansson teaches reduced Streptococcus pneumonia type 5 capsular polysaccharide that has reduced degradation and browning on storage.

The applicants respectfully submit that the structure of the resulting conjugate and its properties are not obvious from the serotype 5 conjugates as disclosed by Moreau, for the pH conditions (for the first process) and the succession of the three steps including a fragmentation step (for the second process) disclosed in the present application and that yield the presently claimed conjugates having no detectable compound X are non-obvious variations of the optimized conventional methods for reductive amination.

As discussed above, when a conventional reductive amination method is performed on pneumococcus type 5 capsular polysaccharide, the Sug residue of the base unit of the pneumococcus type 5 polysaccharide is converted into three compounds: N-acetylated β-D-quinovosamine, N-acetylated β-D-fucosamine, and a compound termed "compound X." Compound X is undesirable because it decreases the immunogenicity of the pneumococcus type 5 capsular polysaccharide (p. 7, lines 10-17). Pneumococcus type 5 capsular polysaccharide subject to conventional reductive animation manifests a ^{13}C NMR signal between 13 and 14 ppm, inclusive (p. 5, l. 37 – p. 6, l. 20) and/or a peak between fucosamine and pneumosamine in an HPAEC-PAD chromatogram.

An aspect of the present invention is methods that avoid formation of compound X. One method comprises reductive amination in the presence of a reducing agent selective for a Schiff base for a period between 30 min. and 4 hours in the pH range of 4 and 6.5, longer periods of time resulting in the formation of the undesirable compound X. P. 8, ll. 19-25 and p. 17, ll. 14-34. A second method involves three successive steps: 1) reduction of the ketone function of the Sug moiety, 2) fragmentation of the reduced polysaccharide, and 3) reductive amination. P. 8, ll. 27-35 and p. 19, l. 16 *et seq.* Accordingly, a ^{13}C NMR signal between 13 and 14 ppm (p. 5, l. 37 – p. 6, l. 20) and/or a peak between fucosamine and pneumosamine in an HPAEC-PAD chromatogram are not observed.

Following the methods of the present application, one obtains the claimed conjugates, which have no detectable compound X.

As noted above, Moreau does not teach such methods and, therefore, does not teach the aminated CP5 presently claimed. Rather, Moreau combines microwaving with methods of amination that, but for the duration of the amination, are otherwise conventional.

And Jansson does not compensate for the deficiencies of Moreau:

1) Jansson describes only the structure of CP5, not the structure of an aminated CP5; and

2) Jansson's borohydride reduction of CP5, underlined in the Office Action, is made to stabilize the CP5 itself, as it has reduced degradation and browning on storage. There is nothing in Jansson teaching that borohydride reduction could be used for preparing an aminated CP5. Furthermore, there is nothing in Jansson teaching or suggesting that borohydride reduction of CP5 could be combined with a fragmentation and conventional methods for reductive amination to obtain the aminated CP5 as recited in the presently pending claims.

Thus, even were one to combine the teachings of Jansson and Moreau as suggested by the Office, one would not arrive at the methods disclosed in the present application or, concomitantly, the presently claimed aminated CP5.

Furthermore, there is nothing in Moreau or Jansson, alone or combined, that suggests or provides a reason for one of ordinary skill in the art to seek a method of reductively aminating pneumococcus type 5 polysaccharide in a manner that avoids the formation of the undesirable compound X. The two processes that are described in the present invention could only have been conceptually derived once the person skilled in the art had knowledge of problems relating to the reductive amination of CP5 by conventional methods. In fact, nothing in the prior art, and nothing in Moreau's and Jansson's teachings in particular, indicate that the prior art recognized the problem that the reductive amination of CP5 according to conventional methods leads to the formation of undesirable X compound. Without a recognition of the problem, there would be no reason to modify prior art methods in the manner disclosed in the present application to yield the presently claimed aminated CP5.

For all of foregoing reasons, the applicants respectfully request reconsideration and withdrawal of this obviousness rejection.

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, he is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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